

**REMARKS**

Claims 58-83 are pending after entry of the amendments set forth herein.

Claims 81 and 83 were examined and rejected.

Claims 81 is amended. The amendment was made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection. Support for the amendment is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary location: page 13, lines 16-17. Accordingly, no new matter is added.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

**Claim rejection under 35 U.S.C. § 101**

Claims 81 and 83 are rejected under 35 U.S.C. § 101 being directed to non-statutory subject matter. The Applicants respectfully traverse this rejection.

The Applicants respectfully submit that the rejected claims recite an *exogenous* scaffold, which, as discussed in the definition for “exogenous scaffold” set forth on page 13, lines 11-17, does not naturally occur in the cell in which it is present. It follows that the cells recited in the claim are not naturally occurring. Accordingly, since the claim recites non-naturally occurring cells, the claim cannot read on a naturally occurring method as the Office asserts.

However, without any intention to acquiesce to the correctness of this rejection and solely to expedite prosecution, claim 82 has been amended to recite a *non-naturally occurring* scaffold.

The Applicants respectfully submit that this rejection has been addressed and may be withdrawn.

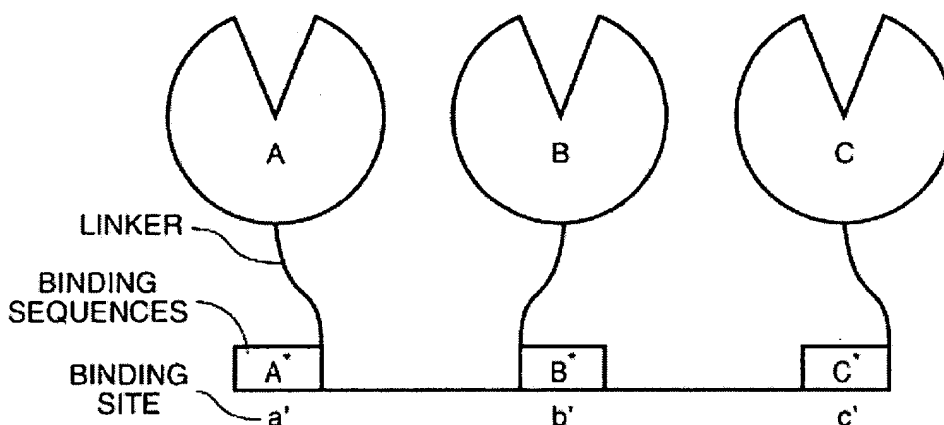
**Rejection under 35 U.S.C. §112, first paragraph (written description)**

Claims 81 and 83 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

This rejected appears to be based on the Office’s assertion that the specification does not provide enough detail about the claim-recited enzymatic complexes.

The Applicants respectfully submit that what is being claimed is a simple and elegant method for complexing, within a cell, enzymes that would not usually be complexed together.

The claim-recited enzymatic complexes are most easily described with reference to Fig. 1A, reproduced below for the Examiner's convenience. Essentially, an enzymatic complex contains two components: a component containing enzymes (referenced as A, B and C in the figure), and a component containing a scaffold (shown as the horizontal line at the bottom of the figure). The enzymes bind to the scaffold via binding sequences (shown as A\*, B\* and C\* or in the figure) in a cell to form an enzymatic complex. This is all that is required to make a claim-recited enzymatic complex.



In discussing the level of disclosure required in a patent application, the MPEP is explicitly clear: a patent specification need not teach, and preferably omits, what is well known in the art.<sup>1</sup>

The Applicants respectfully submit that all of the components necessary for producing enzymatic complexes are well known in the art, and, accordingly, need not be described in any great detail. For example: many thousands of enzymes and their encoding polynucleotides are known and described in the NCBI's PubMed and Genbank database. In fact, many enzymes of particular interest are listed on page 14, lines 1-18 of the instant specification. Likewise, many hundreds of sites of protein/protein or protein/DNA interactions are well characterized and well known in the art and can be used in the subject methods. Polypeptide scaffolds, at a minimum, contain binding sites complementary to those present on

<sup>1</sup> MPEP at § 2164.01 "A patent need not teach, and preferably omits, what is well known in the art." citing *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

the enzymes used, and, as such, could be instantly envisioned by a skilled artisan once a particular binding site had been chosen. Further, if it is desirable to use linkers (such as in the embodiment shown in the figure shown above), such linkers are also well known and described on page 23, lines 6-23 of the instant specification. Methods of introducing binding sites into polypeptides by recombinant means and methods of introducing nucleic acids into cells have been practiced for years. In summary, a claim-recited enzymatic complex can be produced using methods and components that are well known. Accordingly, and in view of the MPEP's guidance regarding the level of disclosure required for a patent application set forth above, the Applicants respectfully submit that methods and components required to produce a enzymatic complex does not need to be discussed in great detail in order to meet the written description requirements for patentability.

In other words, given the massive amount of knowledge of enzymes and interaction sites (e.g., sites of protein/protein interaction), and the fact that methods for introducing binding sites into polypeptides have been practiced for many years, the Applicants respectfully submit that a figure such as Fig. 1A (or Fig. 3 for that matter), in combination with the detail present in the text of instant specification, is sufficient to show that the inventors possessed the invention.

In view of the foregoing discussion, the Applicants respectfully request withdrawal of this rejection.

**Claim rejection under 35 U.S.C. § 112, second paragraph**

Claims 81 and 83 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for omitting essential steps.

The Office notes that the compositions used in the subject methods are limited, and asserts that it is not clear which steps occur prior to the screening step. The Office makes no suggestion of the steps that are omitted.

The Applicants respectfully submit that claim 81 solely recites a single step: screening. No steps are required to occur prior to the screening step. The Applicants respectfully request that the Office elaborates on which steps appear to have been omitted from the claim to allow the Applicants to address the Office's concerns. In particular, the Applicants note that the claims are directed to a method of *screening* using a particular library, not a method of *making* that library. Steps that the Office may refer to, e.g., like "providing a library" or "introducing a nucleic acid into cells", are not required because the

claimed method uses cells that already contain the enzymatic complexes. Adding these steps would be redundant and unnecessary, as well as limiting.

The Applicants respectfully request that this rejection has been adequately addressed and may be withdrawn. If the rejection is to be maintained, then the Applicants respectfully request a first Office Action since this rejection is insufficiently detailed to be addressed, i.e., the rejection states that there are steps missing from the claim but give no clue as to what those steps are.

The Office also asserts that it is unclear whether screening is for an enzymatic complex or for a plurality of cells.

Without any intention to acquiesce to the correctness of this rejection and solely to expedite prosecution, the phrase “for an enzymatic complex that confers an altered phenotype upon a cell” has been deleted from the preamble of claim 82. The method relates to a method of screening a plurality of cells.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

#### **Rejection under 35 U.S.C. §102**

Claims 81 and 83 are rejected under 35 U.S.C. § 102(e) as being anticipated by Khosla (U.S.P.N. 6,391,594). The Applicants respectfully traverse this rejection.

Khosla’s methods involve a polyketide synthase polypeptide (PKS) having multiple enzymatic domains separated by a scaffold. The domains may be exchanged in order to modulate the enzymatic activities, and produce different polyketides.

As noted by the Office, Khosla’s methods involve modifying only the enzymatic activities of a naturally occurring PKS and leaving the PKS scaffold intact. Accordingly, Khosla’s scaffolds are naturally occurring scaffolds, not non-naturally occurring exogenous scaffolds, as required by the claims.

Further, Khosla’s describes only enzymatic complexes in which the enzymes and scaffold of the complex are joined together in *cis*, i.e., in a single fusion polypeptide. Khosla fails to disclose an enzyme complex in which enzymes are bound to a scaffold via binding sequences that are present in the scaffold and enzymes, as required by the instant claims.

Accordingly Khosla fails to teach at least one element of the rejected claims.

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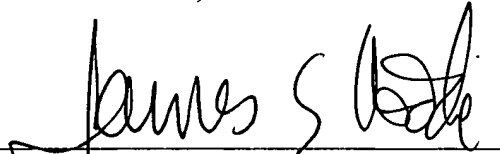
In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

USSN: 08/873,601

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-014.

Respectfully submitted,  
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